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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/009,809	04/26/2002	Ronit Eisenberg	24025-501	1519

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EXAMINER	
NOLAN, PATRICK J	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 04/08/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/009,809	EISENBERG ET AL.	
	Examiner	Art Unit	
	Patrick J. Nolan	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 January 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *44-46,50 and 52-62* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *44-46,50 and 52-62* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1-18-05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

1. Claims 44-46, 50, 52-62 are pending.

2. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 1-18-05 has been entered.

3. It is noted the International Search Report, reference C2 on the IDS submitted 1-18-05 has been considered but has been crossed because it is not appropriate for printing on the face of an issued U S Patent.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to

consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 44-46, 52-60 are rejected under 35 U.S.C. § 103 as being unpatentable over Kuby et al., (U), in view of Aridor et al. (V), and U.S. Patent 5,807,746 (A).

Kuby et al., teaches that inhibition of mast cell degranulation, i.e. histamine release, is a known mechanism to treat allergies, specifically nasal allergy (allergic rhinitis).

The claimed invention differs from the prior art teachings by the recitations of using a cell importation peptide linked to a mast cell degranulation inhibitor peptide to treat allergies.

However, Aridor et al., teaches the use of two peptides KENLKDCGLF, derived from the C-terminus sequence of Gαt, or KNNLKECGLY and each of their use in inhibiting mast cell degranulation as measured by histamine release when it was given to cells that were permeabilized (see page 1570, column 1, second full paragraph, and citation 21 on page 1571, in particular). The '746 patent teaches adding the sequence AAVALLPAVLLALLAP to any known biologically active peptide, by a peptide covalent bond to allow the transportation of said peptide to the inside of the cell, since the permeabilization of cells for peptide entry is only practical for ex vivo therapy, while using importing peptides allows for in vivo therapies. The '746 patent teaches administering said peptides to the skin, orally, or by inhalation (see column 4, in particular).

One of ordinary skill in the art at the time the invention was made would have been motivated to add the importation peptide taught by the '746 patent to the either of the mast cell degranulation inhibitor peptides taught by Aridor et al., because treating allergies with mast cell degranulator inhibitors was well known in the art as taught by Kuby et al., and Aridor et al's peptides suffered from not being useful due to its inability to be transported across the cell membrane, a deficiency cured by the teachings of the '746 patent. From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole is prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references. Further it would have been obvious to use both peptides to treat

allergies since both were demonstrated independently to be effective at inhibiting mast cell degranulation.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 44, 52-62 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for using the importation peptide AAVALLPAVLLALLAP, does not reasonably provide enablement for the use of any importation molecule to treat allergies. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

A requirement to practice the claims is that any fusion protein generated be able to a first inhibit histamine release in an in vitro cell system. However, as disclosed on page 13 of the specification, the import peptides VTVLALGALAGVGVG and RQPKIWFPNRRKPWKK showed no inhibition of histamine release. Since, Applicant's working examples demonstrate unpredictability in the ability of the import peptide to successfully transfer the inhibitory degranulation peptide to mast cells in vitro it would require an undue amount of experimentation to practice the full scope of the claimed invention in vivo.

Furthermore, Applicant has recited the use of the peptides to treat multiple sclerosis. As noted the by The Merck Manual of Diagnosis and Therapy, 17th edition, mast cell degranulation is not recognized to be involved in causing the pathology of MS. Since there are no working examples demonstrating the use of the claimed peptides in treating MS, and the state of the art does not recognize that MS's pathology is caused by mast cell degranulation, it would be unpredictable to treat a patient with MS with a compound that inhibits mast cell degranulation and expect it to work when it is not art recognized that MS's pathology is caused by mast cell degranulation.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 44, 50 and 52-60 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

claim 44, line 6 recites "whereby the complex molecule", however the term "complex" is not previously recited in the claim. Clarification is required.

Claim 50 recites an agent that has two parts, the first part causes importation of the second part into mast cells. It further defines the second part as including the cell importation sequence (AAVALLPAVLLALLAP). This is confusing. Clarification is requested. Furthermore, the claim recites SEQ ID NO: 7 and cyclic derivatives thereof and then further recites the molecule further comprises cyclization between lysine at position 17 and the C-terminus of the peptide. This again is confusing. Does applicant intent the claim to recite a cyclized SEQ ID NO. 7, that is then further cyclized at position 17? Clarification is required. Lastly, claim 50, line 6 recites "whereby the complex molecule", however the term "complex" is not previously recited in the claim. Clarification is required.

7. The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

8. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patrick Nolan whose telephone number is 571-272-0847.

If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Christina Chan, can be reached at 571-272-0841.

Patrick J. Nolan, Ph.D.

Primary Examiner, Group 1640

March 22, 2005